PSA Screening and diagnosis

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Disclosures

- Advisory board
  - Janssen
  - Bayer
  - MSD
  - BMS

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The controversy of PSA screening

- 2 large RCTS
  - ERSPC
  - PLCO

- Smaller screening studies
  - Goteborg
  - Stockholm
  - Noorkoping

ERSPC

- PSA screening on PCa mortality
- 7 EU countries, n=182,000 men
- PSA testing every 4 years
- Age 50-74 years
- Latest – 13 years

- Screening variation between centres
  - Sweden screen every 2 years, Belgium every 7 years
  - On average, men screened 2.3 times

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Lancet. 2014 December 6; 384(9959): 2027–2035

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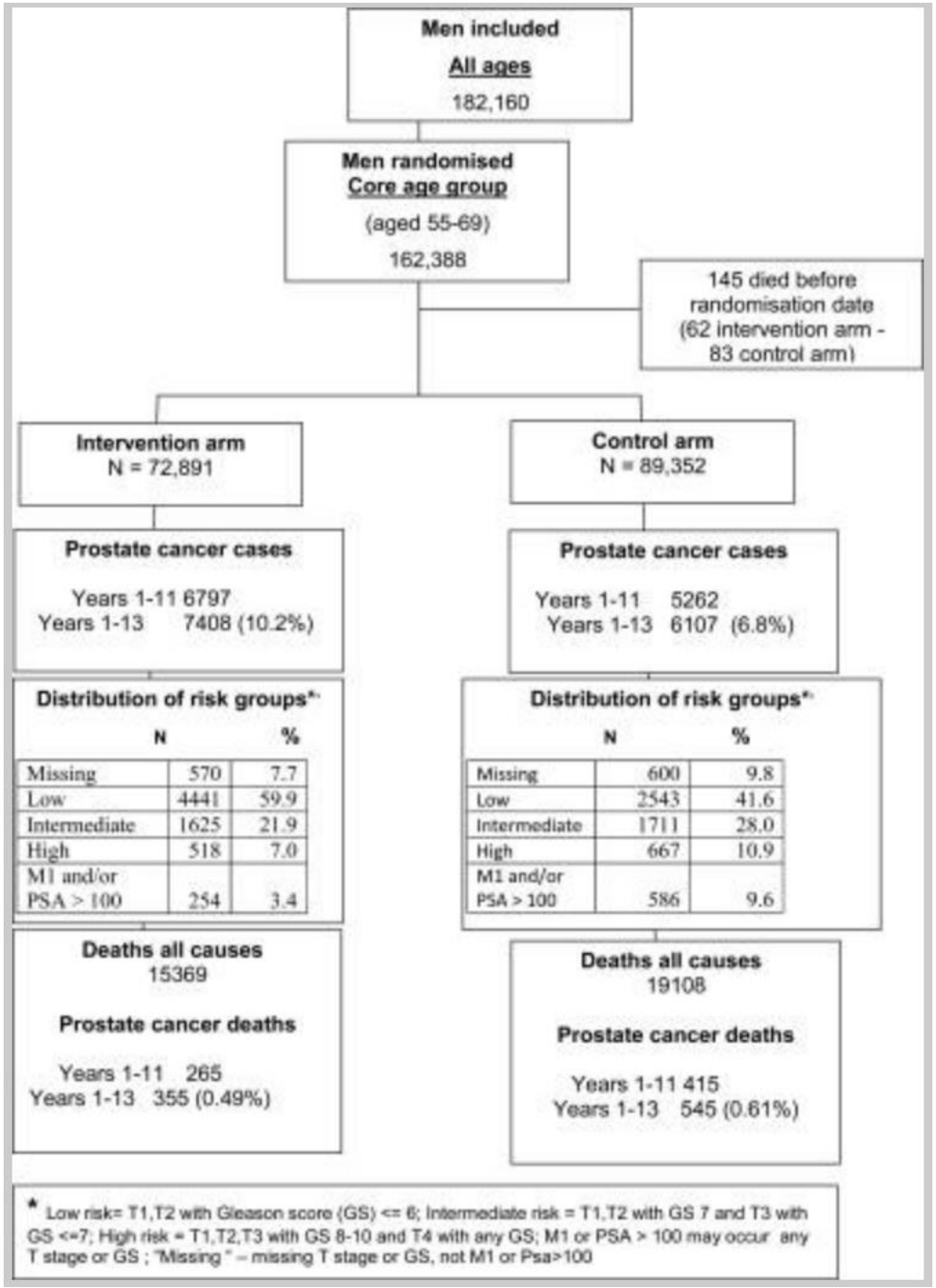

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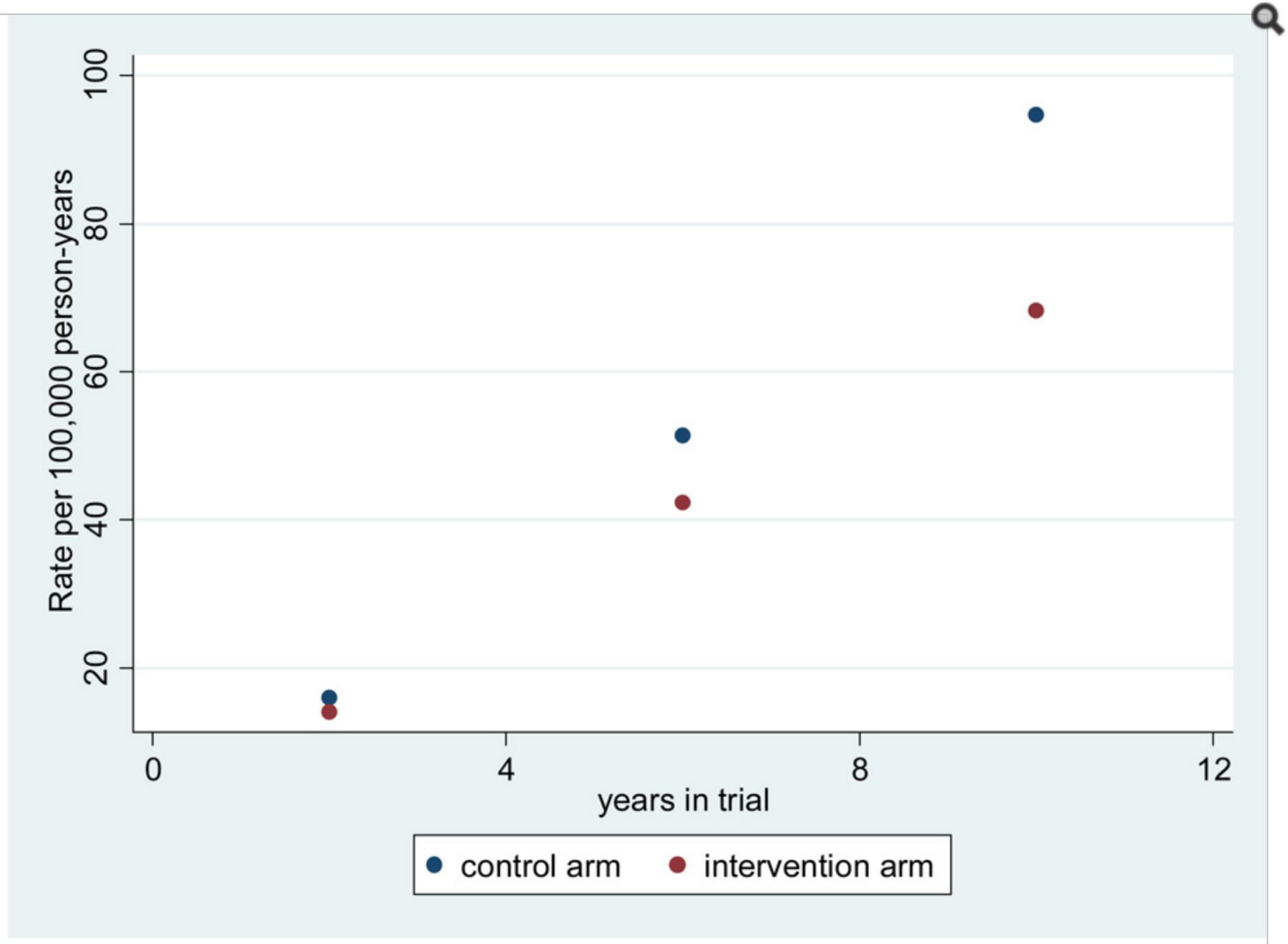
- PCa mortality between screen and control
- HR 0.79 (95% CI 0.69-0.91, p=0.001)
- Relative RR 21%
- Absolute RR 1.28 per 1000 men randomised

- NNI (invite) 13 years – 781
- (11 years – 979, 9 years – 1410)

- NND (detect) 13 years - 27
- (11 years – 35, 9 years - 48)

Figure 3



PC Mortality rate in each arm by 4 year period

- 75% of those who underwent biopsy for elevated PSA – no cancer within 1 year
- Average 20% PSA screen contamination
  - 8.6% Spain to 36% Italy
- Exclusion Polish and French data
- 41% of the 4235 cancers > screening arm were detected outside protocol
  - ? Frequency of PSA testing every 4 years

PLCO

- PCa mortality by PSA screening
- N=76 685 men, 55-74 years
- PSA year, DRE every 2 years
- PSA >4 , abnormal DRE - > trigger ’usual care’

- Opportunistic screen if requested by patient

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J Natl Cancer Inst 2012;104:125–132

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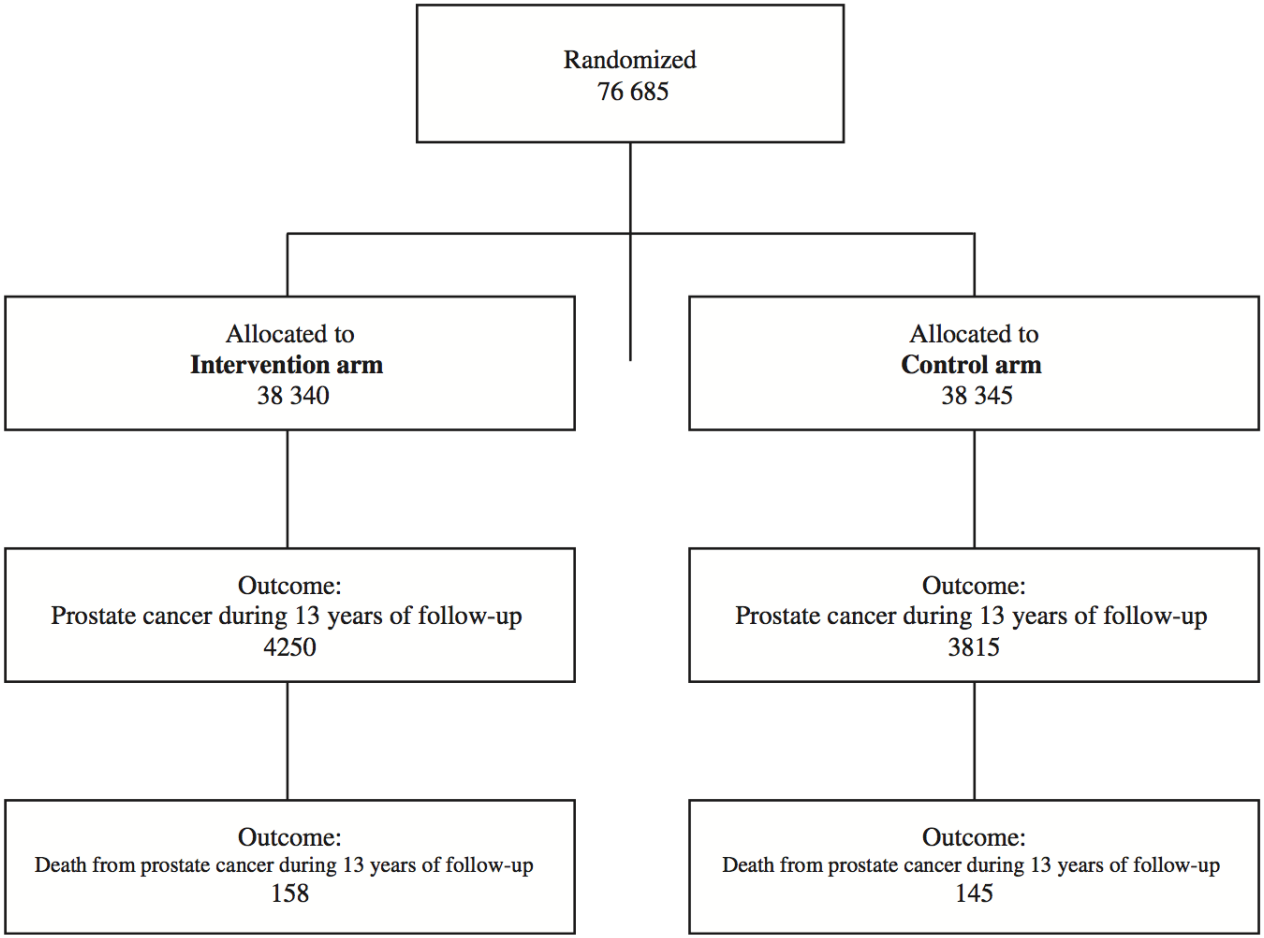

Figure 1. Flow diagram for male participants in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

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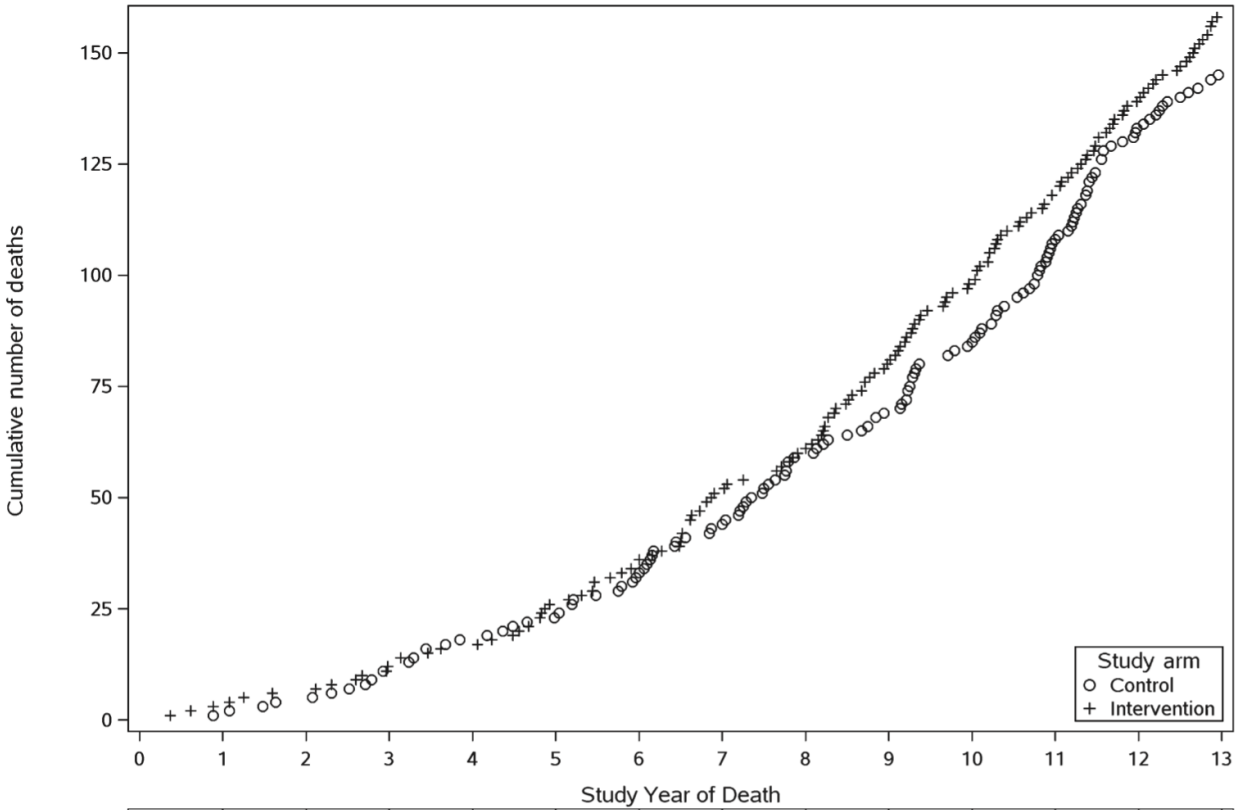

Cumulative deaths - I	3	6	12	16	26	36	51	61	80	98	118	140	158	*
Cumulative PY - I	38 217	76 112	1 13 629	1 50 725	1 87 382	2 23 541	2 59 118	2 94 052	3 28 048	3 59 768	3 87 164	4 09 535	4 26 977	*
Cumulative deaths - C	1	4	11	18	23	33	44	59	69	85	108	133	145	*
Cumulative PY - C	38 223	76 132	1 13 635	1 50 689	1 87 278	2 23 329	2 58 811	2 93 631	3 27 455	3 58 904	3 86 109	4 08 262	4 25 439	*

Figure 3. Cumulative deaths from prostate cancer in the intervention and control arms from year 1 to year 13. C = control arm; I = intervention arm; PY = person-years.

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Table 1. Comparison of Randomized Prostate-Cancer Screening Trials.*

Data	PLCO	ERSPC
Median follow-up (yr)	13	11
PSA screening interval	Annually for 6 yr	Every 2 to 4 yr
Nonattendance (%)	15.0	17.4
Contamination (%)†	85	24
Difference in rate of PSA testing between study groups (%)‡	0	58.6
Prerandomization PSA testing (%)	44	Not reported
Rate ratio for death from prostate cancer in men undergoing randomization to screening vs. usual care (95% CI)	1.09 (0.87–1.36)	0.79 (0.65–0.98)

* Data are from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial or the European Randomized Study of Screening for Prostate Cancer (ERSPC) unless noted otherwise. CI denotes confidence interval, and PSA prostate-specific antigen.

† Data on contamination are from Pinsky et al.[2] for the PLCO screening trial and from Kerkhof et al.[3] for the ERSPC.

‡ The difference in the rate of PSA testing between study groups refers to the difference in the rate of testing between those who underwent randomization to usual care and those who underwent randomization to screening.

Goteborg

- PSA screening on PCa mortality
- Randomised, population- based prostate screening

- N=20,000, age 56-64
- Median f/u 14 years
- PSA testing every 2 years
- PSA threshold 3.0 (ERSPC level)

- Above threshold - > DRE, sextant TRUS biopsy

- Diagnosis of cancer tracked via West- Swedish Regional Cancer Registry

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Lancet Oncol. 2010 August ; 11(8): 725–732

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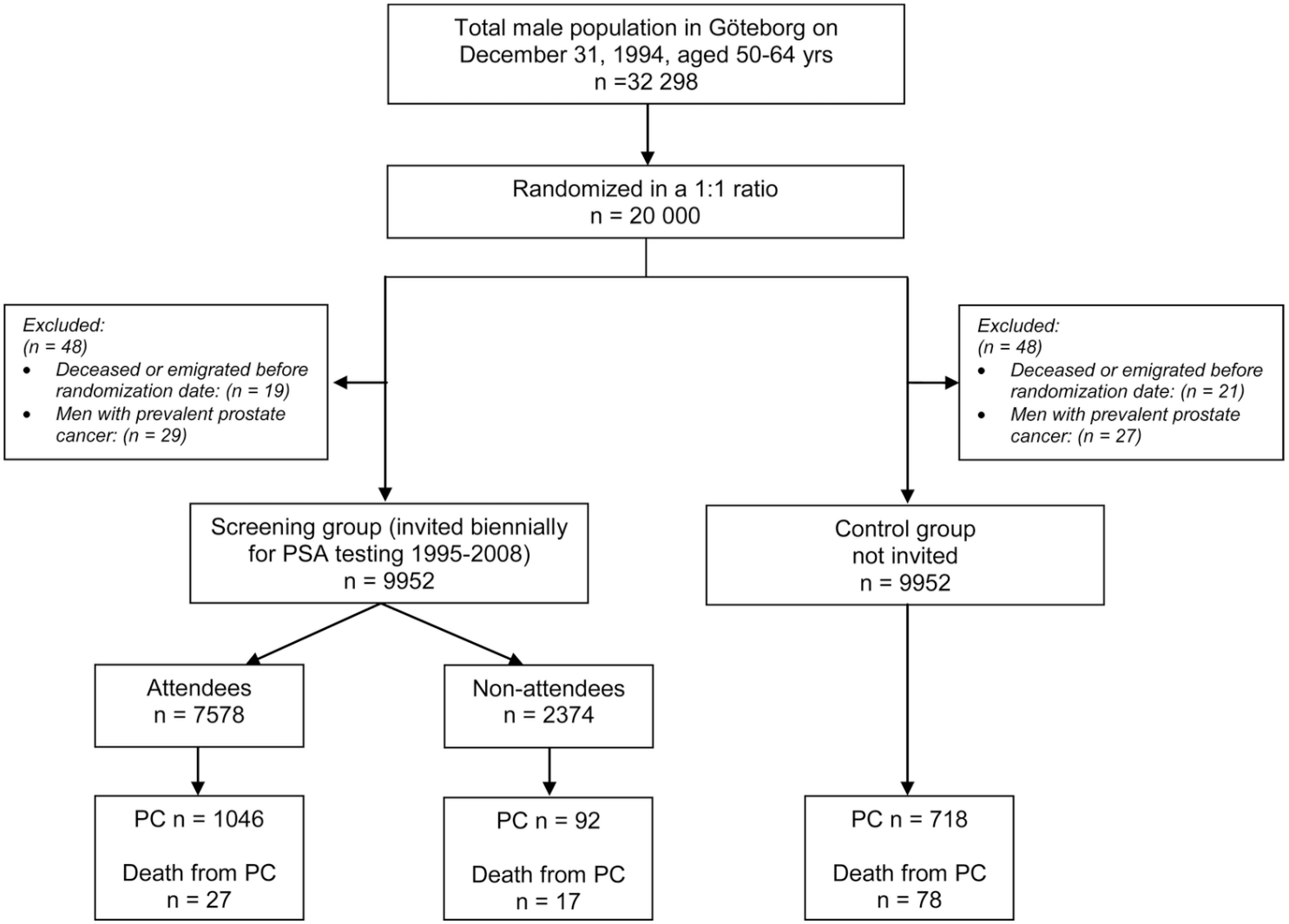

Figure 1.
CONSORT diagram of the study

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Goteborg

- Incidence PCa – 12.7% vs 8.2%
- (HR 1.64, 95% CI 1.5-1.8, p<0.0001)

- NNS – 239
- NND – 12
- 1 PCa mortality

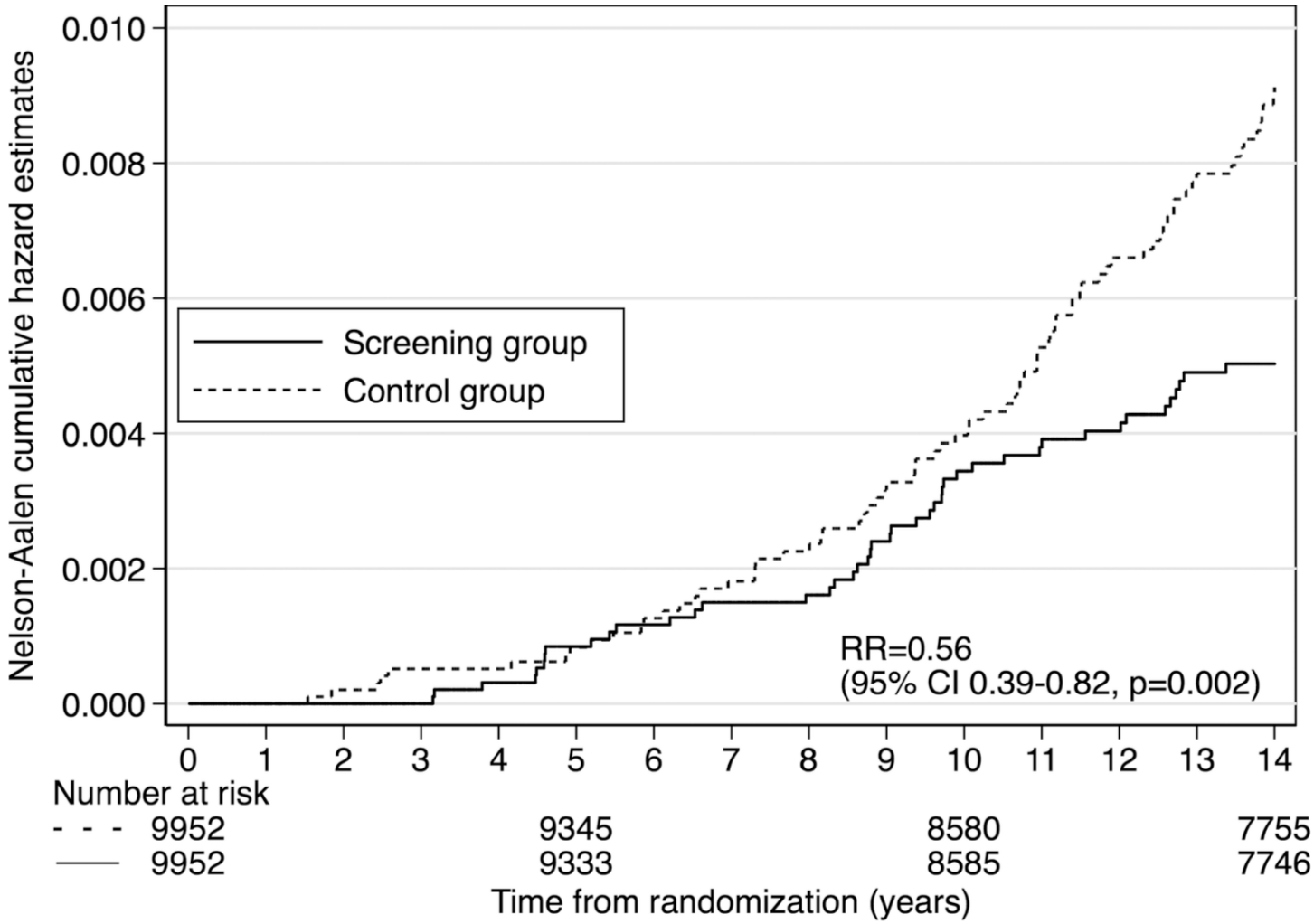

Figure 3.
Cumulative risk of death from prostate cancer using Nelson-Aalen cumulative hazard estimates

A summary of evidence so far…

- PSA screening general population
  - 50 years onwards
  - PSA > 3
  - 2 to 4 yearly
- Reduction in PCa mortality
- Overdiagnosis and treatment
  - 1 in 239 to 781 screen
  - 1 in 12 to 27 diagnosis

Public health policy (1)

- 2012 US Task Force
- Grade D recommendation
- Recommend against routine PSA testing
- All ages

Public health policy (2)

- AUA
  - consider screening 55-69 years
  - 40-55 years – discussion, personalised
  - 2 yearly PSA

- ACS
  - Consider screen >50 years for average age
  - >40 years for African American or family history
  - Baseline PSA determines frequency

- EAU
  - Consider screen at 40s, then decide frequency

- Follow ‘Level 1’ evidence ?
- Personalised decision on screening?

Baseline PSA

- Copenhagen City Heart Study
- 4383 men aged 20-94 yr from the Danish general population
- PSA was measured in plasma samples obtained in 1981-1983
- Median follow-up was 18 yr

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Eur Urol. 2012 May;61(5):865-74

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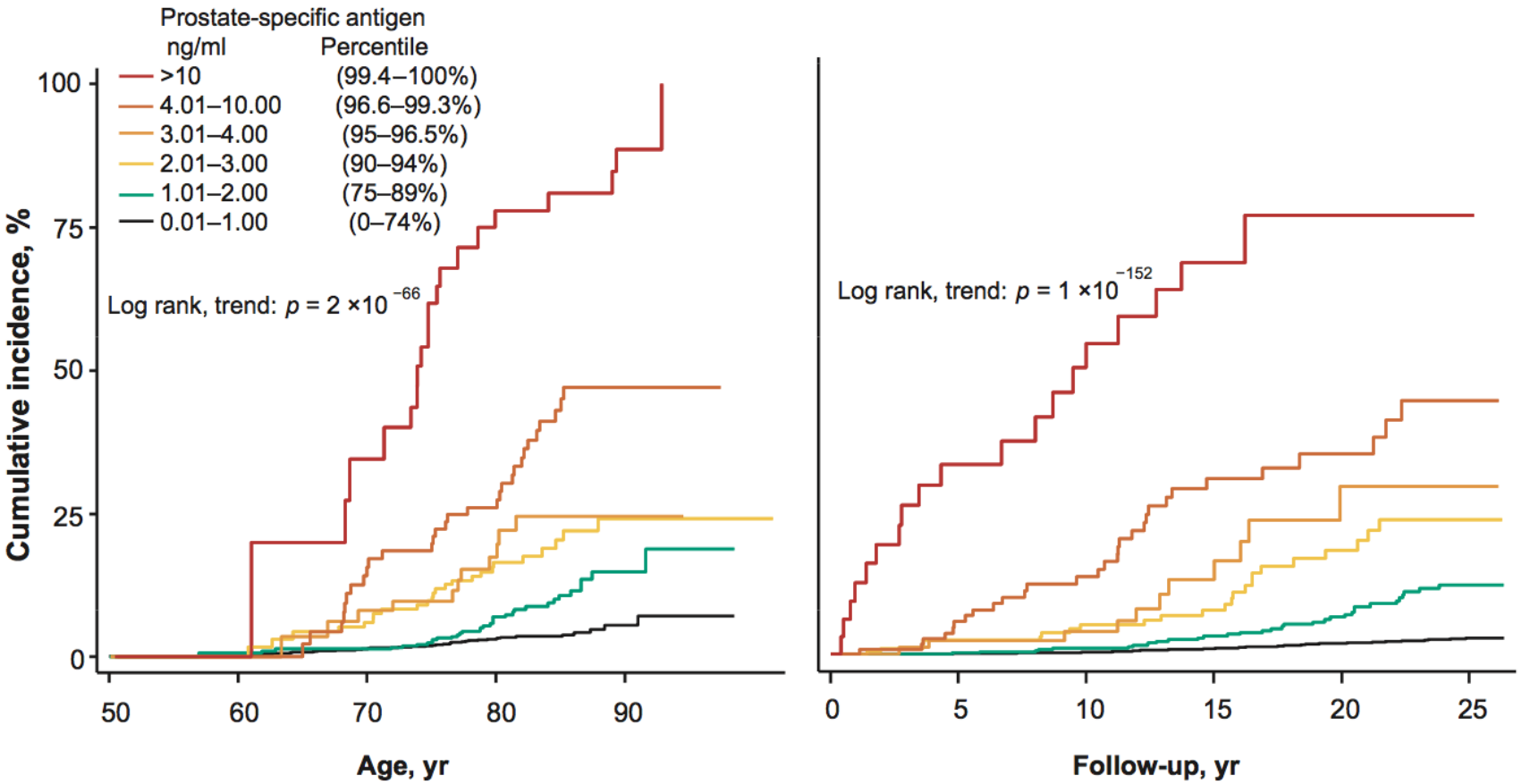
Prostate cancer



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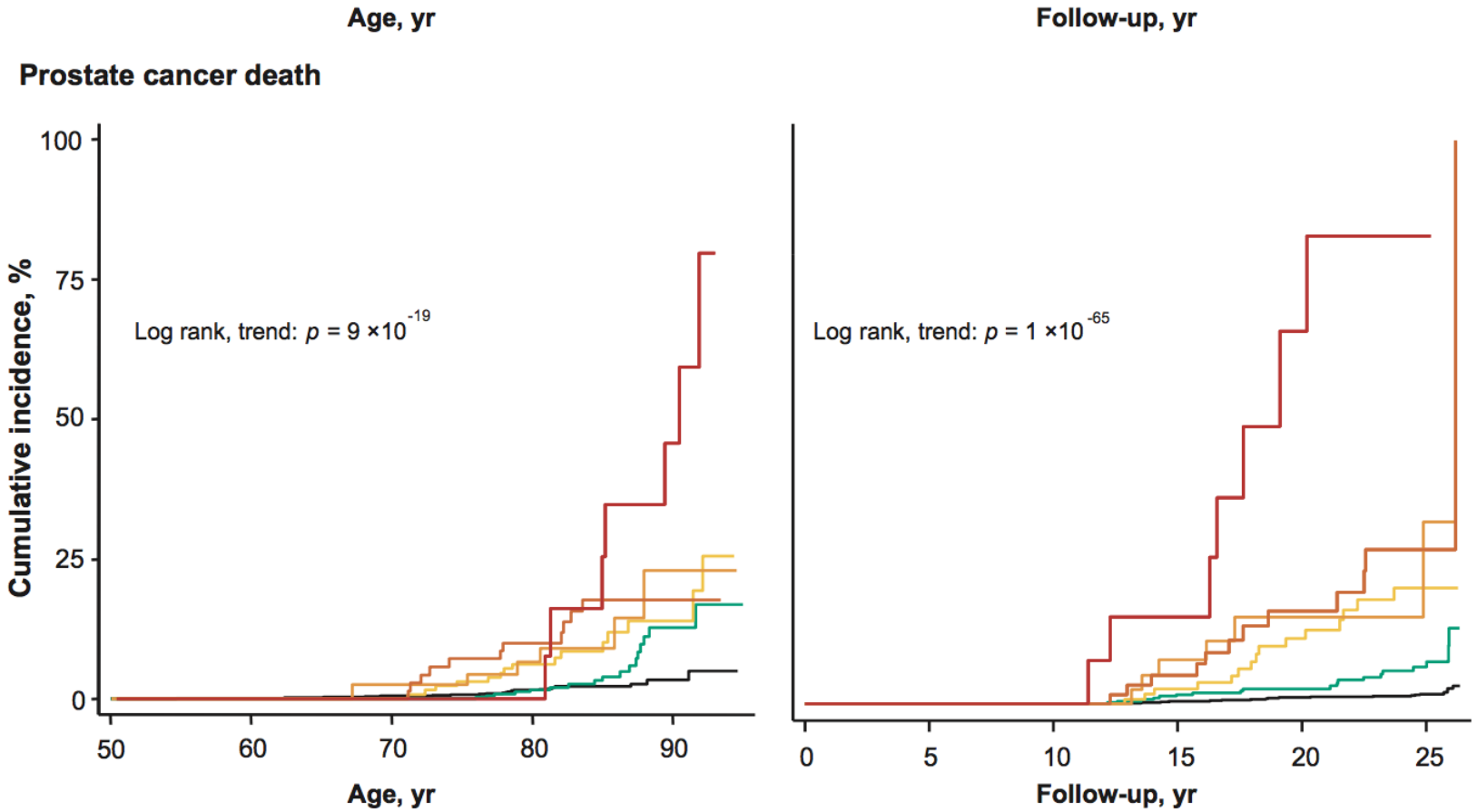

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Baseline PSA Midlife

- 40-59 years old US physicians,
- N=22, 071
- Physician's Health Study
- Aspirin vs B-carotene trial

- 234 PCa, 711 age-matched controls

- Median PSA (controls)
  - 40-49 years (0.68 ng/ml)
  - 50-54 years (0.88)
  - 55-59 years (0.98)

- Risk of lethal PCa if PSA >90th percentile per age group
  - OR 8.7 (1.0 to 78.2) - 40 to 49 years
  - OR 12.6 (1.4 to 110.4) 50 to 54 years
  - OR 6.9 (2.5 to 19.1) 55 to 59 years

A population-based stratified approach…

- PSA screening general population
  - ~~– 50 years~~ onwards *40 years*
  - ~~– PSA > 3~~ *baseline PSA*
  - – 2 to 4 yearly *depending on baseline PSA*

To your next patient…

- A discussion of pros and cons is mandatory
- Level 1 evidence not sufficient for decision about screening
- Benefits
  - PCa mortality
  - Metastatic disease
- Cons
  - Over diagnosis
  - PSA cripple

Using PSA variants

Comparison Between the Four-kallikrein Panel and Prostate Health Index for Predicting Prostate Cancer

Tobias Nordström [a, b], Andrew Vickers [c], Melissa Assel [c], Hans Lilja [d, e, f], Henrik Grönberg [b], Martin Eklund [b, g]

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https://doi.org/10.1016/j.eururo.2014.08.010

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MRI Fusion-Targeted Transrectal Prostate Biopsy and the Role of Prostate-Specific Antigen Density and Prostate Health Index for the Detection of Clinically Significant Prostate Cancer in Southeast Asian Men

To cite this article:
Tan Teck Wei, Png Keng Siang, Lee Chau Hung, Yuwono Arianto, Yeow Yuyi, Chong Kian Tai, Lee Yee Mun, Tan Cher Heng, and Tan Yung Khan. Journal of Endourology. September 2017, ahead of print. https://doi.org/10.1089/end.2017.0485

BJU International. 115():2, MAR 2015
Issn Print: 1464-4096
Publication Date: 2015/03/01

Share Print

Prospective evaluation of the utility of %P2psa and the Prostate Health Index (PHI), in predicting prostate cancer in initial prostate biopsies of Singaporean men, with total PSA between 4.0 and 10 ng/ml: COP-07

Y. S.B. GOH; G. L.L. TAN; Y. K. TAN; B. C. TAIDagger;; K. M.L. TAN; R. C.W. HAWKINS; F. HONG; E. CHIONG

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Optimising biopsy outcomes

- Reduction of morbidity

- Increasing accuracy of biopsy
  - Needle placement
  - Image guidance

Morbidity of TRUS Biopsy

- Infection -> hospitalisation

- 3% locally
- Up to 6 % internationally

- Antibiogram and antibiotics strategy

- Trans-faecal biopsy

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EUROPEAN UROLOGY 64 (2013) 876–892

Annals of the Academy of Medicine Singapore Volume 38, 2009, Pages 212-216

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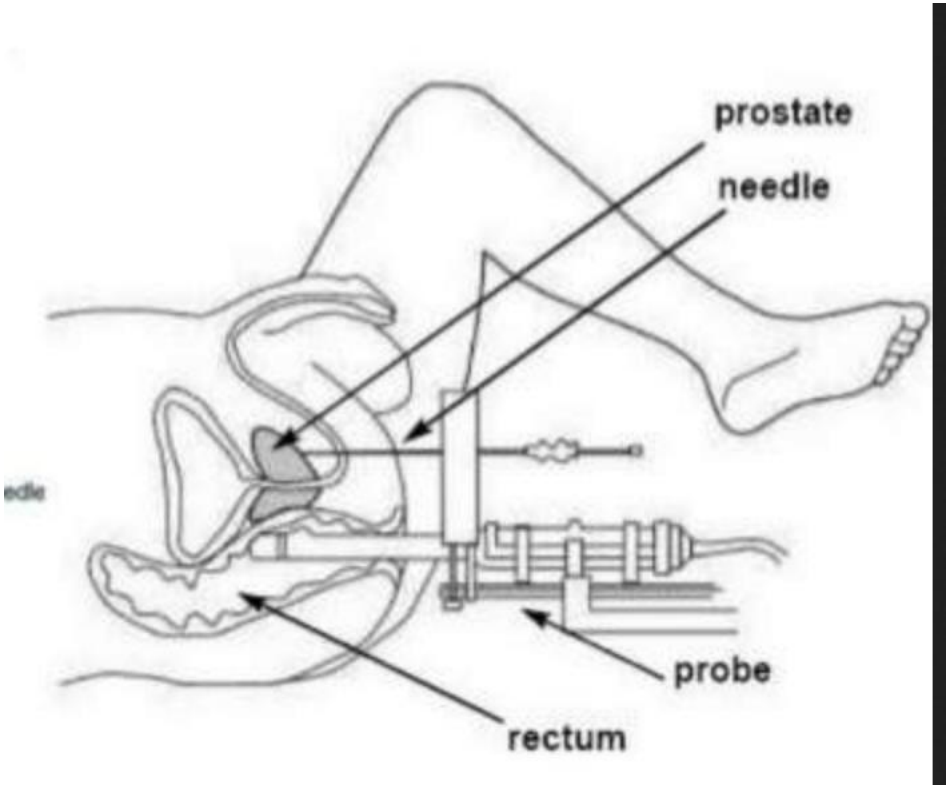
Morbidity of TRUS Biopsy

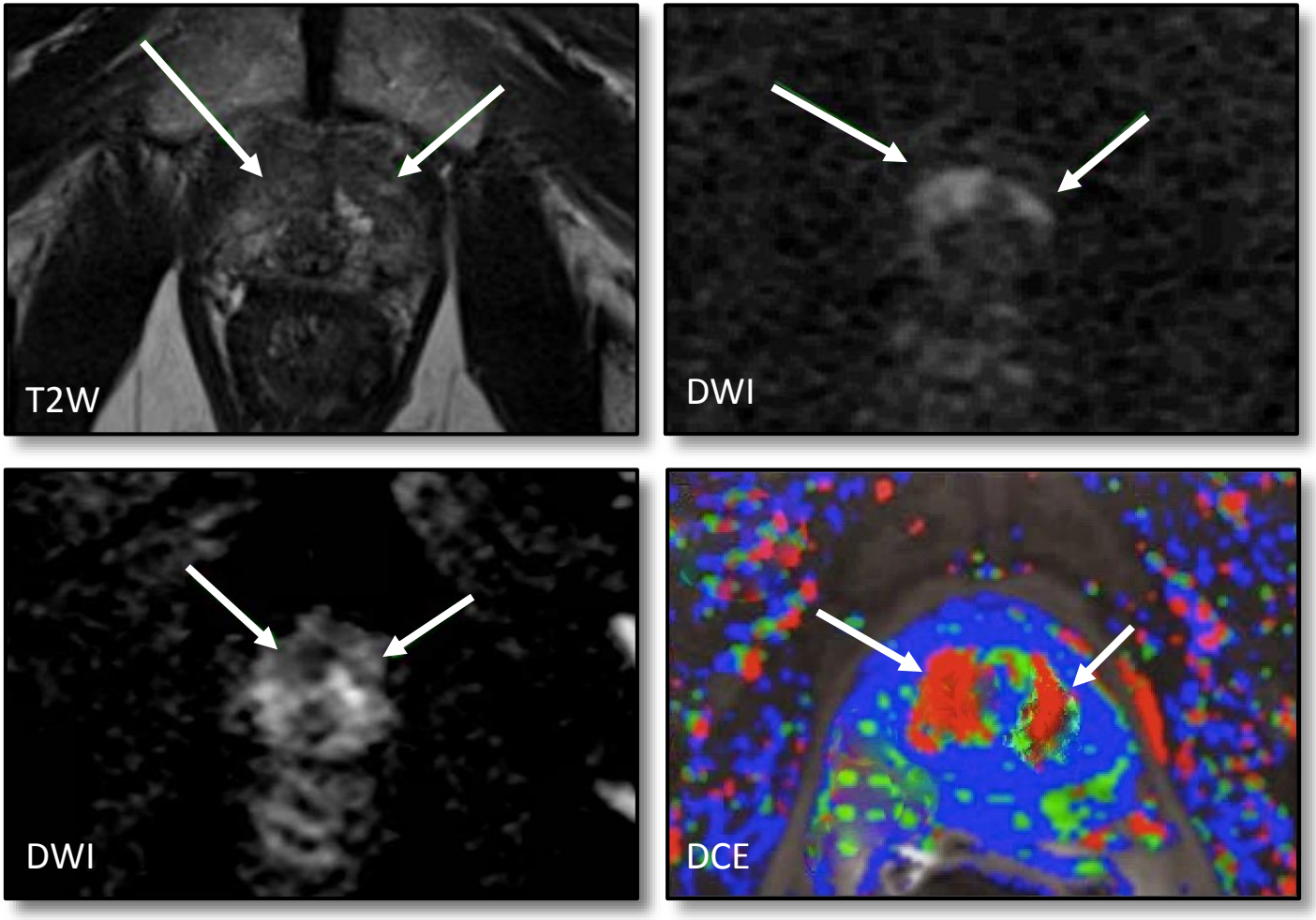
- Rectal bleeding (1-45%)
- Haematuria
- LUTS (up to 25%)
- Haemospermia (up to 90%)

Transperineal biopsy



Accuracy of biopsy

- MRI- US Fusion biopsy
- PIRADS classification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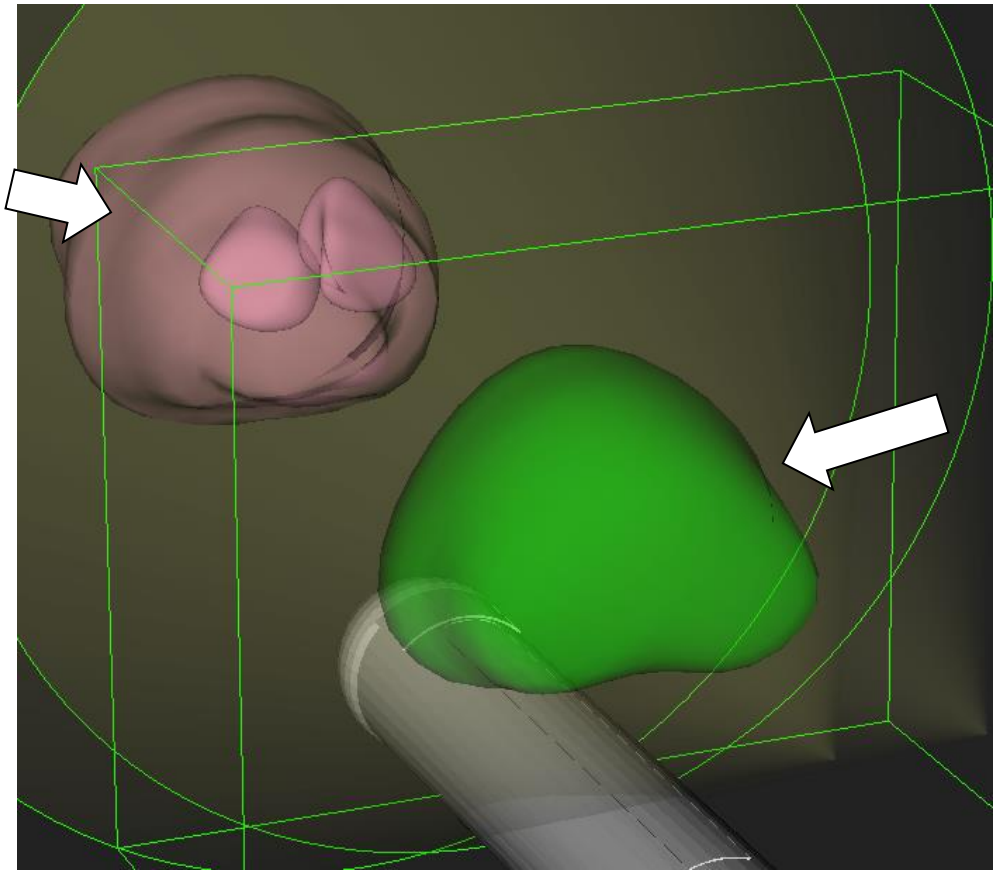
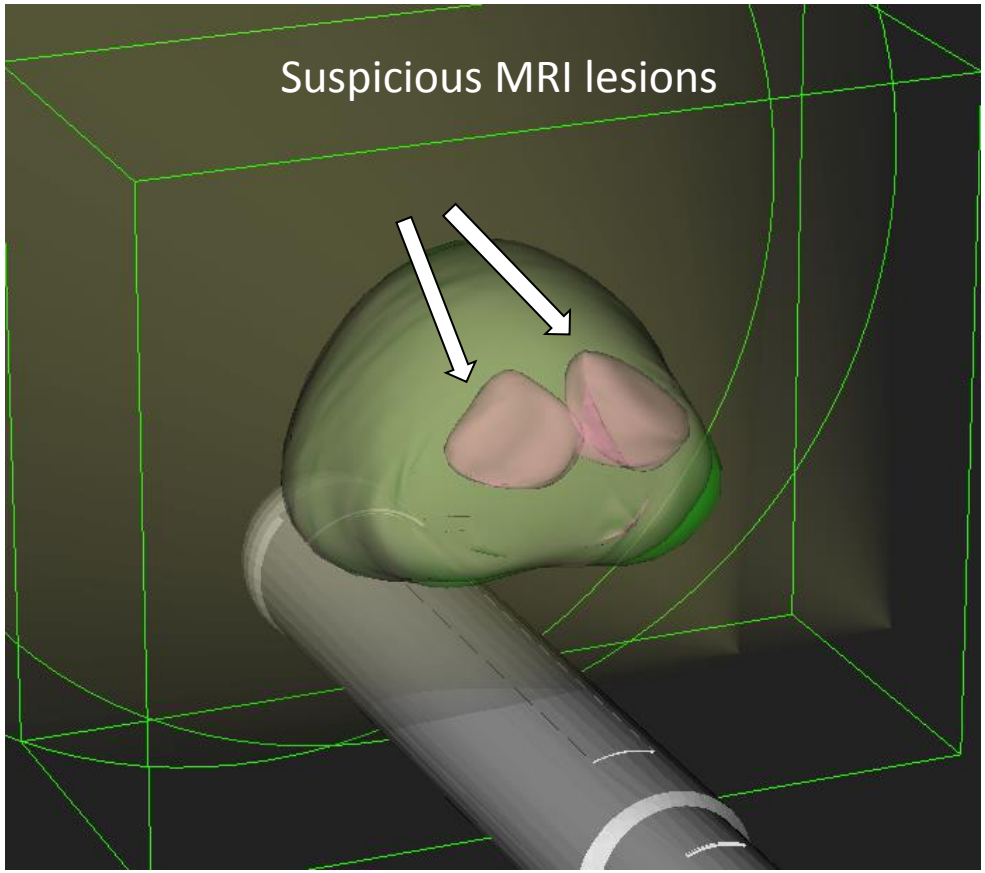
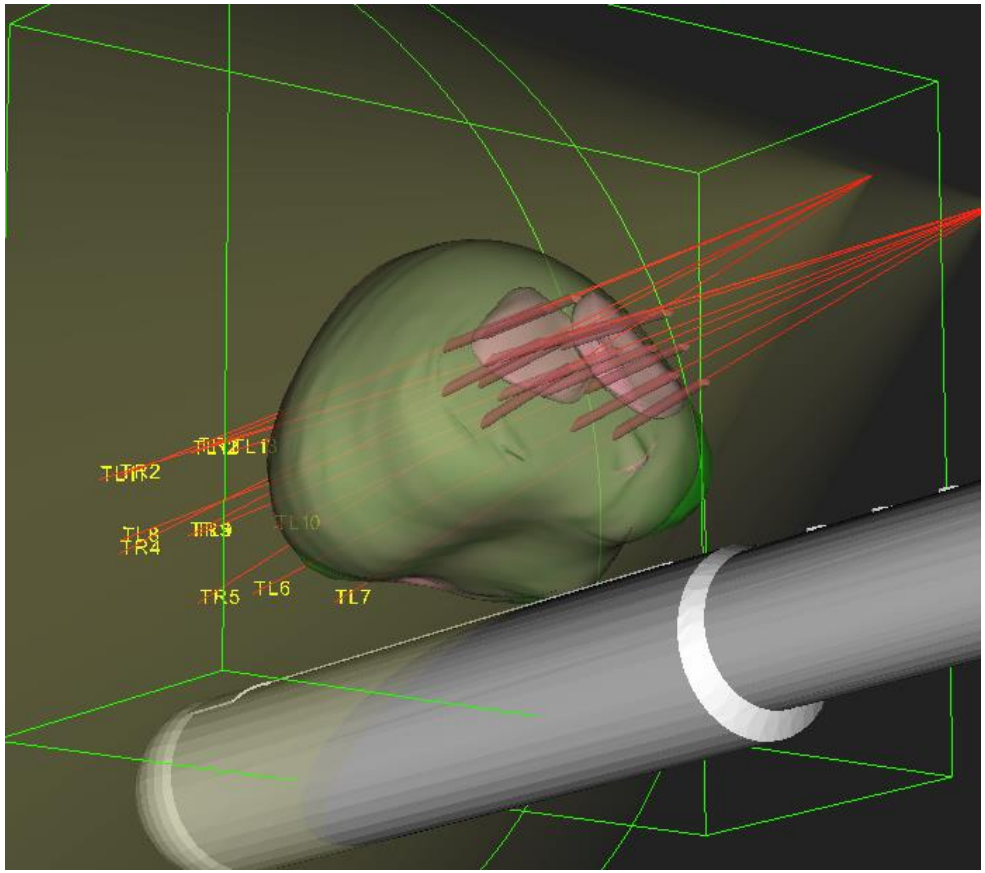



Suspicious MRI lesions


TL8
TR4
TR5
TL6
TL7

Utility of Imaging

- MRI PIRADS v2
- 3T MRI T2 weighted, DWI and DCE
- Cost of MRI??
- PSA variants cheaper but less yield in long run(?)

FIGURE 1

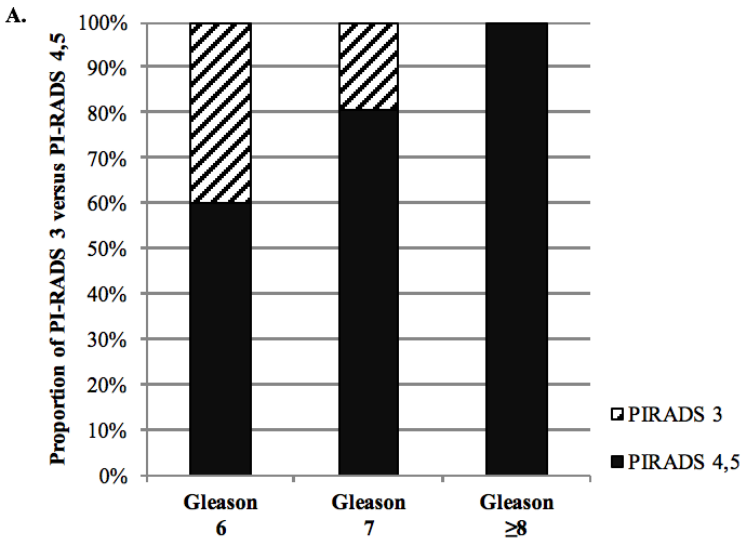
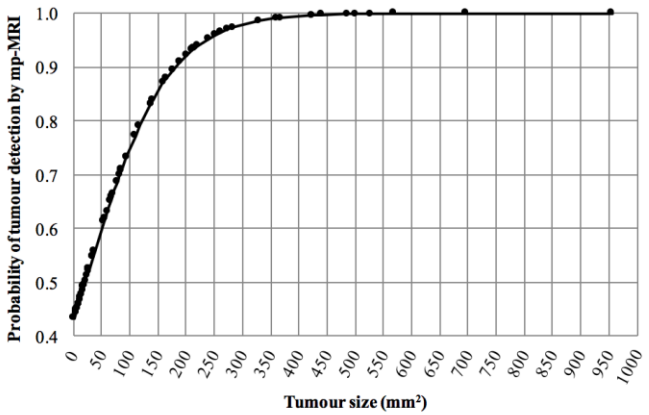


FIGURE 2



International Journal of Urology. 23():79, JUL 2016

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Take Home Messages

- PSA screening reduces PCa mortality
- Screening strategy
  - Personalised , no ideal one as of now
  - Use baseline PSA at middle age to decide, 40-50 years??
  - Family history, race
- Optimising prostate cancer diagnosis reduces NNS
  - Image guided biopsy
  - Reducing morbidity of procedure

- PSA variants may be helpful to decide earlier biopsy

Content

What is PSA?
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Diagnostic tests
Treatment options
Active surveillance
Medical source data
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Your Prostate Cancer Risk Calculator

The Prostate Cancer Risk Calculator has been designed to help you, and the health professionals looking after you. There are eight different calculators and the first two are designed for individual use without any medical knowledge.

You can first assess your general risk by using **Risk Calculator 1 (no PSA result available)** which takes into account your age, family history and urinary symptoms.

What is PSA and why is it important?
You may already have had a simple test to measure the level of prostate specific antigen (PSA) in your blood. The chance of having prostate cancer goes up as the level increases. Once you know your PSA level, you can then use **Risk Calculator 2 (using your PSA result)**. It will help you make a more informed decision about whether it would be wise to undergo further tests.

Even if your PSA is higher than normal, it does not mean you have prostate cancer, because other diseases of the prostate may increase its level. It is important to know that some cancers are slow growing, cause minimal symptoms and are not life threatening.

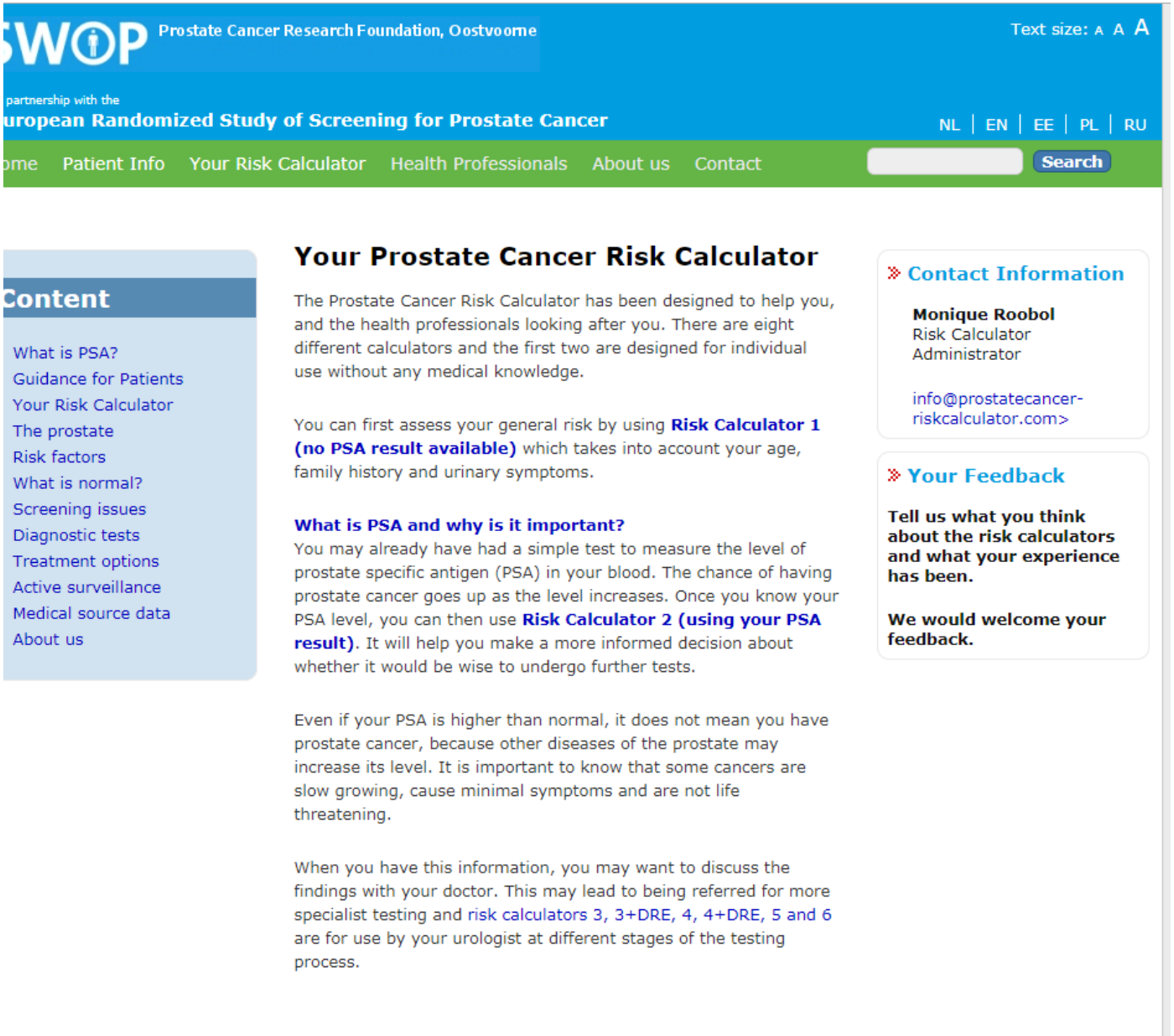
When you have this information, you may want to discuss the findings with your doctor. This may lead to being referred for more specialist testing and risk calculators 3, 3+DRE, 4, 4+DRE, 5 and 6 are for use by your urologist at different stages of the testing process.

Contact Information

Monique Roobol
Risk Calculator Administrator

info@prostatecancer-riskcalculator.com>

Your Feedback

Tell us what you think about the risk calculators and what your experience has been.

We would welcome your feedback.